

REMARKS

Status of the claims:

With the above amendments, claims 28-33, 36, and 50-51 have been canceled, claims 60-73 have been added, and claims 42-44 and 53-54 have been withdrawn from a prior restriction requirement. Thus, claims 34, 35, 37-49 and 52-73 are pending. No new matter has been added by way of the above amendments. Claims 60-73 have support at page 5, lines 8-10. Reconsideration is respectfully requested in light of the following remarks.

Inquiry about the status of claim 52

Applicants respectfully inquire about the status of claim 52. In the Office Action of January 27, 2004, the Examiner indicated that claim 52 was withdrawn from consideration. However, in the Office Action of June 13, 2003, the Examiner examined this claim. Thus, Applicants respectfully ask that the Examiner clarify the status of this claim.

Method and Process Claims

Applicants have added method of use claims 60-73 to the instant application. Applicants respectfully request that the Examiner consider these claims together with the compound

claims, consistent with the holding in *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995). Moreover, also consistent with *Ochiai*, Applicants respectfully request rejoinder of the claims directed to the process of making the compound(s).

Rejections under 35 USC §112, first paragraph

Claims 42-44 and 53-54 are rejected under 35 USC §112, first paragraph as not being enabled. The Examiner asserts that SO_2F is not a recognized leaving group. Applicants believe that the Examiner meant $-\text{OSO}_2\text{F}$. Applicants, herein, provide an enclosure (consisting of two pages) from J. March, *J. Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, Fourth Edition, 1992, New York, p. 353 showing $-\text{OSO}_2\text{F}$ as a potential leaving group. Applicants also respectfully submit that in claim 44 when q is 1 to 4 the leaving group would be $-\text{OSO}_2\text{C}_q\text{F}_{2q+1}$, which are triflate compounds or a derivate molecule, which are known in the art to be good leaving groups. Further, attached, please find a reference from *The Merck Index*, Twelfth Edition, ed. Budavari et al. 1996, Whitehouse Station, New Jersey, p. ONR-89, showing the Suzuki coupling wherein $-\text{OSO}_2\text{C}_q\text{F}_{2q+1}$ is shown as a leaving group. With these showings, Applicants believe that the enablement rejection has been obviated. One of skill in the art would recognize that

-OSO₂C_qF_{2q+1}, are good leaving groups. Withdrawal of the rejection is warranted and respectfully requested.

Claim Objections

Claim 36 is objected to as being a substantial duplicate of claim 34 or claim 35. Applicants have canceled claim 36 so this rejection is moot. Withdrawal of the objection is warranted and respectfully requested.


With the above remarks and amendments, Applicants believe that the claims, as they now stand, define patentable subject matter such that passage of the instant invention to allowance is warranted. A Notice to that effect is earnestly solicited.

If any questions remain regarding the above matters, please contact Applicant's representative, T. Benjamin Schroeder (Reg. No. 50,990), in the Washington metropolitan area at the phone number listed below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By 

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Attachments: J. March, *J. Advanced Organic Chemistry, Reactions, Mechanisms and Structure*, Fourth Edition, 1992, New York, p. 353 (two pages)

The Merck Index, Twelfth Edition, ed. Budavari et al. 1996, Whitehouse Station, New Jersey, p. ONR-89 (two pages)

ons have been offered.³²⁵ One is repulsion between the adjacent is stabilized by the extra pair of es solvation of the nucleophile.³²⁸ as no alpha effect in the reaction HO_2^- shows a strong alpha effect t a carbonyl or other unsaturated nucleophile with a carbocation,³³¹ at a saturated carbon.³³²

ff more easily the more stable it d the best leaving groups are the ong the halides and fluoride the cleophilic substitution is always is effect is that OH and OR are an come off when the groups are

Reactions in which the leaving ve been called $\text{S}_{\text{N}}1\text{cA}$ or $\text{S}_{\text{N}}2\text{cA}$, n $\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$ process (these dsnds for conjugate acid, since the strate. The IUPAC designations d $\text{A}_{\text{h}} + \text{A}_{\text{N}}\text{D}_{\text{N}}$; that is, the same ary step. When another electro- ed instead. The ions ROH_2^+ and atures in super-acid solutions.³³⁴

I^-) cannot take part in $\text{S}_{\text{N}}1\text{cA}$ or conjugate acids under the acidic ause $\text{S}_{\text{N}}1$ reactions do not require , most of them take place under

Tetrahedron Lett. **1982**, 23, 615; Hoz; Buncel s is not the sole cause, see Oae; Kadoma iselin; Terrier *Tetrahedron Lett.* **1984**, 25,

J. Chem. Soc., Chem. Commun. **1985**, 1406; ncks *J. Am. Chem. Soc.* **1990**, 112, 1951. 3, 105, 2481; Buncel; Um *J. Chem. Soc., t. Fr.* **1988**, 415. For some evidence against un. **1987**, 860.

ano *Bull. Chem. Soc. Jpn.* **1969**, 42, 1110; . **1972**, 37, 1037. Sec, however, Beale *J.* **1982**, 104, 4896, *Int. J. Chem. Kinet.* **1982**,

atai *The Chemistry of the Ether Linkage*;

lamanworth *J. Am. Chem. Soc.* **1967**, 89,

han acting as a nucleophile: Okada; Abe;

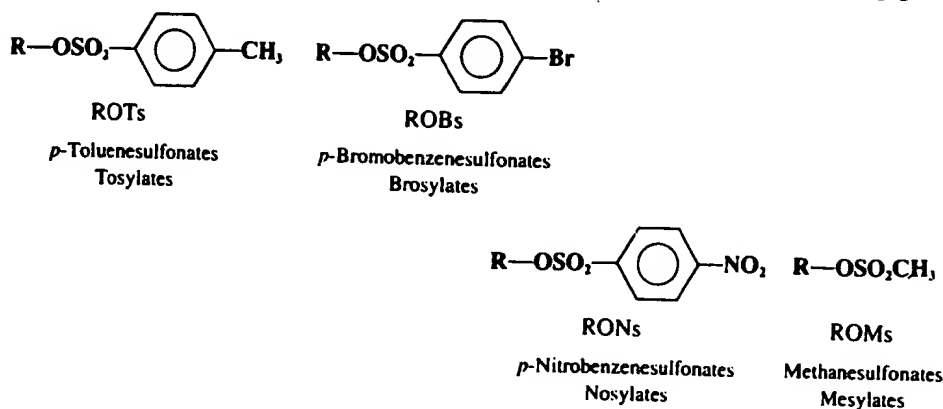
acidic conditions. In contrast, $\text{S}_{\text{N}}2$ reactions, which do require powerful nucleophiles (which are generally strong bases), most often take place under basic or neutral conditions.

Another circumstance that increases leaving-group power is ring strain. Ordinary ethers do not cleave at all and protonated ethers only under strenuous conditions, but epoxides³³⁶ are cleaved quite easily and protonated epoxides even more easily. Aziridines³³⁷ and epi-



sulfides, three-membered rings containing, respectively, nitrogen and sulfur, are also easily cleaved (see p. 368).³³⁸

Although halides are common leaving groups in nucleophilic substitution for synthetic purposes, it is often more convenient to use alcohols. Since OH does not leave from ordinary alcohols, it must be converted to a group that does leave. One way is protonation, mentioned above. Another is conversion to a reactive ester, most commonly a sulfonic ester. The sulfonic ester groups *tosylate*, *brosylate*, *nosylate*, and *mesylate* are better leaving groups



than halides and are frequently used. Other leaving groups are still better, and compounds containing these groups make powerful alkylating agents. Among them are oxonium ions (ROR_2^+),³³⁹ alkyl perchlorates (ROClO_3),³⁴⁰ ammonioalkanesulfonate esters (*betylates*) ($\text{ROSO}_2(\text{CH}_2)_n\text{NMe}_3^+$),³⁴¹ alkyl fluorosulfonates (ROSO_2F),³⁴² and the fluorinated com-

³³⁶For a review of the reactions of epoxides, see Smith *Synthesis* **1984**, 629-656. For a review of their synthesis and reactions, see Bartók; Láng, in Patai *The Chemistry of Functional Groups, Supplement E*; Wiley: New York, **1980**, pp. 609-681.

³³⁷For a review of aziridine cleavages in the synthesis of natural products, see Kametani; Honda *Adv. Heterocycl. Chem.* **1986**, 39, 181-236.

³³⁸There is evidence that relief of ring strain is not the only factor responsible for the high rates of ring-opening of 3-membered rings: Di Vona; Illuminati; Lillocci *J. Chem. Soc., Perkin Trans. 2* **1985**, 1943; Bury; Earl; Stirling *J. Chem. Soc., Chem. Commun.* **1985**, 393.

³³⁹For a monograph, see Perst, Ref. 84. For reviews, see Perst, in Olah; Schleyer, Ref. 92, vol. 5, 1976, pp. 1961-2047; Granik; Pyatin; Glushkov *Russ. Chem. Rev.* **1971**, 40, 747-759. For a discussion of their use, see Curphey *Org. Synth.* **VI**, 1021.

³⁴⁰Baum; Beard *J. Am. Chem. Soc.* **1974**, 96, 3233. See also Kevill; Lin *Tetrahedron Lett.* **1978**, 949.

³⁴¹King; Loosmore; Aslam; Lock; McGarrity *J. Am. Chem. Soc.* **1982**, 104, 7108; King; Lee *Can. J. Chem.* **1981**, 59, 356, 362; King; Skonieczny; Poole *Can. J. Chem.* **1983**, 61, 235.

³⁴²Ahmed; Alder; James; Sinnott; Whiting *Chem. Commun.* **1968**, 1533; Ahmed; Alder *Chem. Commun.* **1969**, 1389; Alder *Chem. Ind. (London)* **1973**, 983. For a discussion of the hazards involved in the use of these and other alkylating agents, see Alder; Sinnott; Whiting; Evans *Chem. Br.* **1978**, 324.

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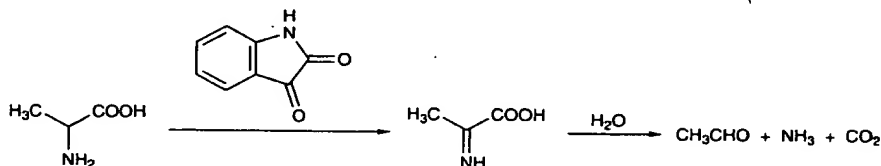
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Organic Name Reactions

366. Strecker Degradation

A. Strecker, *Ann.* **123**, 363 (1862).

Reaction of an α -amino acid with a carbonyl compound in aqueous solution or suspension to give carbon dioxide and an aldehyde or ketone containing one less carbon atom. Inorganic oxidizing agents can also be used to bring about the transformation:

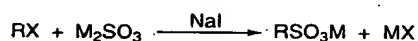


Mechanism: Schönberg *et al.*, *J. Chem. Soc.* **1948**, 176. Reviews: Schönberg, Moubacher, *Chem. Rev.* **50**, 261 (1952); N. van Chuyen *et al.*, *Agr. Biol. Chem.* **36**, 1199 (1972), *C.A.* **77**, 114855e (1972) Photo-promoted hypochlorite oxidation: Y. Ogata *et al.*, *Bull. Chem. Soc. Japan* **54**, 2057 (1981).

367. Strecker Sulfite Alkylation

A. Strecker, *Ann.* **148**, 90 (1868).

Formation of alkyl sulfonates by reaction of alkyl halides with alkali or ammonium sulfites in aqueous solution in the presence of iodide:

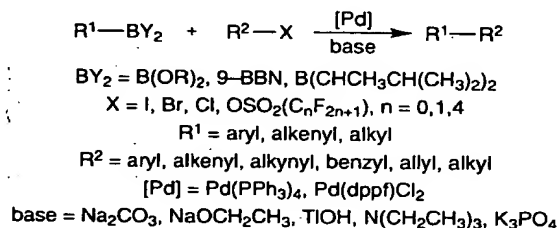


A. Collmann, *ibid.* **101**; W. Hemilian, *ibid.* **168**, 145 (1873); *Ber.* **6**, 562 (1873); *Swiss. pats.* **105,845**; **104,907** (1925); F. C. Wagner, E. E. Reid, *J. Am. Chem. Soc.* **53**, 3409 (1931); C. Weygand, *Organic Preparations* (New York, 1945) p 306; M. Quaedvlieg, *Houben-Weyl* **9**, 372 (1955).

368. Suzuki Coupling

N. Miyaura *et al.*, *Tetrahedron Letters* **1979**, 3437; N. Miyaura, A. Suzuki, *Chem. Commun.* **1979**, 866.

Palladium-catalyzed cross coupling of organic halides or perfluorinated sulfonates with organoboron derivatives proceeding with high stereo- and regioselectivity:

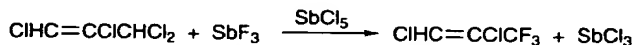


Competition with Heck reaction, *q.v.*, when using an alkenyl boronate ester: A. R. Hunt *et al.*, *Tetrahedron Letters* **34**, 3599 (1993). Alternative palladium catalysts: G. Marck *et al.*, *ibid.* **35**, 3277 (1994); T. I. Wallow, B. M. Nowak, *J. Org. Chem.* **59**, 5034 (1994). Reviews: A. Suzuki, *Pure Appl. Chem.* **63**, 419-422 (1991); A. R. Martin, Y. Yang, *Acta Chem. Scand.* **47**, 221-230 (1993). Cf. Hydroboration Reaction; Stille Coupling.

369. Swarts Reaction

F. Swarts, *Bull. Acad. Roy. Belg.* **24**, 309 (1892).

Fluorination of organic polyhalides with antimony trifluoride (or zinc and mercury fluorides) in the presence of a trace of a pentavalent antimony salt:



A. L. Henne, *Org. React.* **2**, 49 (1944); M. Hudlicky, *Chemistry of Organic Fluorine Compounds* (MacMillan, New York, 1962) pp 93-98.

370. Swern Oxidation (Moffatt-Swern Oxidation)

K. Omura, D. Swern, *Tetrahedron* **34**, 1651 (1978).

Mild oxidation of primary and secondary alcohols, promoted by oxalyl chloride activation of dimethyl sulfoxide, evidently involving the dimethyl alkoxy-sulfonium salts. Upon the addition of base, the intermediates rearrange intramolecularly to generate aldehydes or ketones, respectively:

